REMARKS/ARGUMENTS

Rejections Under 35 U.S.C. § 102

Claims 2, 3, 16, 18, 20-23 and 25-31 are rejected under 35 U.S.C. § 102(e) as being anticipated by Karg et al. (U.S. Patent No. 6,706,538).

This rejection is overcome at least for the following reasons.

Karg is not prior art to the instant invention. Specifically, the instant invention is a 371 National Phase entry of international application PCT/GB00/01029 filed on March 20, 2000 which claims priority to GB 9906477.6 filed March 19, 1999. Karg has a filing date of June 12, 2000 claiming priority to U.S. Provisional application No. 60/185810 filed February 29, 2000. Thus, Karg cannot anticipate the instant invention because the instant invention was filed almost a full year before Karg. This priority date is correctly documented on the published international application and the priority documents itself was filed with the Office upon national phase entry and is in the FILE WRAPPER available in PAIR having a mail room date of September 19, 2001. The rejection is therefore moot and should be withdrawn. Applicant respectfully requests same.

Rejections Under 35 U.S.C. § 103

Claims 2-3, 16, 18, 20-23 and 25-31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Coffman et al.

This rejection is overcome, at least, for the following reasons.

The Combination Of Coffman With An Ordinary Skill Would Not Work

Claims 18, 25 and 31, from which all other claims depend each *require* that the liquid is dispensed in drops in the range of from between 10 to 500 *nanoliters*. Coffman specifies that the volume of liquid transferred is in the range of 5 to 150 *microliters* two to three orders of magnitude difference. Coffman, Col. 6, line 13. This is further pointed out by the Office in the action where it is stated that the 384 well plate might only hold 120 µl. Therefore, Coffman

cannot make obvious the instant invention, because Coffman is incapable of expelling liquid in the volume *required* by the claims.

Coffman Is Incapable Of Dispensing Volumes Of Liquid In Any Discrete Volume

As explained in the instant specification, those of skill in the art recognize that expulsion of such precise fluid volumes are difficult to achieve. As discussed the surface tension of liquids does not allow the discharge of such small volumes until such volume reaches the order of 10 to 50 microliters. Thus, the instant invention solves this problem by ejecting liquid through outlet port 6 via the application of a discrete gas volume through cannulae 28.

The Combination Made By The Office Would Not Work

As stated in the specification, one purpose of the instant invention is for use in automating reactions such as DNA sequencing reactions, immuno assays and the like, where very small discrete volumes of reagents are required. Spec (WO 00/56455) at pg. 6, lines 3-5. Those of skill in the art of DNA sequencing reactions, for example, recognize that the volumes of each reagent used in a reaction must be consistent and repeatable. The instant invention provides this ability via a gas pulse that is transferred to the cartridge via cannulae 28. Ejection volumes are controlled by altering the gas pulse. See, pg. 8, line 1 – pg. 9, line 13. The apparatus of the instant invention thus provides for the ejection of discrete volumes of reagents in the range of 10 to 500 *nanoliters* as recited in the specification and required by the claims.

In contrast, Coffman discloses only a system which allows a microtiter plate having x number of wells to sit on top of a second microtiter plate having y number of wells wherein y is $\geq$ x. The means by which Coffman transfers liquid from plate x to y is via a vacuum manifold 70 connected to plate y – the lower plate. See fig. 15 and Col. 9, lines 10-24 and Col. 6, lines 35-38. E.g., the liquid in the upper plate is pulled from below via the constant negative pressure of the vacuum. Thus, Coffman provides absolutely no ability to even identify volumes as small as one microliter, much less 5 nanoliters as is required by the claims and, further, to repeatedly expel such volumes into a desired reservoir. This is, in fact, recognized explicitly by Coffman, "Gasket 30 fills the space between drip directors 16 depending from the 96-well plate. Thus, when the 96-well plate is aligned over a respective set of wells of the 384-well plate, gasket 30 will automatically cover open wells of the 384-well plate to prevent cross-contamination of the

wells during transfer of material to the selected well set and/or to prevent the drawing of air through the open wells when a vacuum is applied to the outlets of the 384-well plate, thereby preventing drying of the wells." Coffman, Col. 8, lines 10-14. For this reason alone the rejection is overcome and should be withdrawn.

Further, Coffman states that the apparatus can simultaneously transfer and filter the fluid. Specifically, "this invention provides for the direct transfer of samples from a first well plate . . . to a second well plate . . . while simultaneously filtering the sample a purifying the resultant material." Col. 7, lines 10-13. This is further recognized by Coffman:

> As a variation or further option, the amount of air passing through the open wells in the 384-well plate may be further reduced by providing a wetted porous material such as a membrane or frit 60 atop, for example, a purification media 62 packed in each well 23 as shown in FIG. 12. Media 62 is disposed over an additional frit 64 placed in the bottom end of each well. Frit or membrane 60 is assumed to have a pore size fine enough so that when wetted it does not allow air to easily pass through. For example, pore sizes for frit 60 could be between 0.1 μm and 10 μm. As a further advantage to this enhancement, provision of a porous material such as a frit or membrane on top of the purification media within the wells of the 384-well plate also serves to distribute more evenly by capillary action any reagent added, such as an elution buffer. This is particularly noticeable when *a relatively small volume* of buffer is used." Coffman, Col. 8, lines (emphasis added).

First, applicants point out that the volumes Coffman recites are in the range of 5–150 μl. Second, Coffman discusses the use of a frit 60 for use in evenly distributing media. Anyone of skill in the art recognizes that at volume in the range of 10-500 nanoliters, most of such volume would be lost inside the filter, frit or chromatographic medium and would never be expelled due to hydrostatic forces, etc. Simply put, there would be no reagent left for the reaction. Further, applicants point out that no one of skill in the art would try to purify or separate volumes as small as 10-500 nanoliters, especially when the force used to move the liquid out of its reservoir is a vacuum manifold pulling a liquid from via an exit path. Thus, for this reason the rejection is overcome and should be withdrawn.

As discussed above, Coffman cannot make obvious the instant invention **because Coffman would not work** even when combined with the unspecified art referred to by the

Office. Therefore, the rejections to the invention are overcome and should be withdrawn. Applicant respectfully requests same.

This application now stands in allowable form and reconsideration and allowance is respectfully requested.

This response is being submitted on or before January 18, 2008 making this a timely response. It is believe that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 04-1420. The Examiner is urged to telephone the under-signed if a discussion would be beneficial in furthering prosecution.

Respectfully submitted,

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